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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,481	04/15/2004	Vincent Ling	WYS-00501	7025

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EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,481	LING ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-21* is/are pending in the application.

4a) Of the above claim(s) *3 and 10-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed on 09/24/2007, are acknowledged.

Claims 1 and 3 – 21 are pending.

Claims 3 and 10 – 16 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Inventions/Species, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 04/09/2007.

Claims 1, 4 – 9, and 17 – 21 are presently under consideration.

2. This Office Action is in response to Applicant's amendment and arguments, filed on 09/24/2007.

The rejections of record can be found in the previous Office Action, mailed on 06/22/2007.

The objections and rejections of record have been withdrawn in view of Applicant's amendment and arguments, except as set forth herein.

It is noted that New Grounds of Rejection are set forth herein.

3. Claim 19 is objected to because of an apparent typographical error, in that the reference to the base claims has been deleted. For examination purposes, it is presently assumed that the claim is intended to depend on claim 1.

4. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 4 – 9, and 17 – 21 stand rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement, for the reasons of record. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

A. The specification does not provide a sufficient enabling description of a method of inhibiting proliferation of lymphocytes by contacting the lymphocytes with a "soluble" form of B7-H3.

Applicant's arguments have been fully considered but have not been found convincing. Applicant argues that the amendment to recited "activated" lymphocyte should obviate the rejection of record.

However, in the absence of evidence or reasoning to rebut the rejection of record, it appears that the grounds of rejection set forth in the previous office action are fully applicable to the amended claims.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

B. The specification does not provide a sufficient enabling description of a method of inhibiting proliferation of lymphocytes in a mammal afflicted with or at risk of a generically recited "immunologic disorder." One of skill in the art is aware that immunologic disorders include those which may benefit from inhibition of proliferation of lymphocytes, as well as those which will likely be aggravated by such inhibition (e.g. cancer, or conditions accompanied by insufficient immune responses). Therefore, one of skill in the art is not enabled to practice the method as claimed.

C. The specification does not provide a sufficient enabling description of the claimed method, because the specification does not provide a sufficient enabling description of how to make and use a polypeptide comprising an amino acid sequence which is "at least 90% identical" to the recited sequence, wherein the polypeptide competitively inhibits binding of B7-H3 to its receptor.

Applicant's arguments have been fully considered but have not been found convincing. Applicant argues that the amendment to substitute the recitation "at least 90% identical" for "substantially identical" should obviate the rejection of record.

This is not found persuasive, because the recitation of the genus of polypeptide sequences does not appear to be sufficiently supported by disclosure of three working examples in the instant specification.

In view of the unpredictability of the art, as addressed in the previous office action, the skilled artisan would not reasonably expect a generically recited polypeptide "at lease 90% identical" to B7-H3 to share the same function as B7-H3, and there is insufficient guidance to direct the skilled artisan to such functional sequences. Thus the recitation of percent identity language does not allow the skilled artisan to make and use the recited polypeptides commensurate in scope with the instant claims without undue experimentation.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

6. The following is a quotation of the appropriate paragraphs of **35 U.S.C. 102** that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 4 – 9, and 17 – 20 stand rejected under **35 U.S.C. 102(a) and 102(e)** as being anticipated by Mikesell et al. (US Pat. Pub. No. 2002/0095024; of record; see entire document), for the reasons of record.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that since Mikesell et al. teach that modulation of B7-related factor function may be useful in the induction of tumor immunity, therefore, allegedly, Mikesell et al. do not teach that the sequences SEQ ID NO: 7 or 13 of the reference are useful in *inhibiting proliferation* of a lymphocyte, as recited in the instant claims.

In response, Mikesell et al. teach methods which are not manipulatively different from those instantly claimed, i.e. administering to a subject polypeptides which are within the scope of the instant claims, or contacting lymphocytes in vitro with the same polypeptides. Therefore, the outcome of performing the method steps taught by Mikesell et al. is inherently the same as that of the instantly claimed methods.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

New Grounds of Rejection

8. The following is a quotation of the **second paragraph of 35 U.S.C. 112**.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 4 – 9 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 – 9 are indefinite as being dependent on cancelled claim (claim 2). Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

It is suggested that Applicant rewrite the claims in independent form to include the limitations of base claims. Alternatively, the claims may be amended to depend on other base claims currently under consideration. It appears that claims 4 was intended to depend on claim 1, which dependence is presently assumed for examination purposes.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

10. Claims 1 and 19 – 21 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable one of skill in the art to make and use the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification does not provide a sufficient enabling description of a method of inhibiting lymphocyte proliferation "in a mammal," and in particular a mammal "afflicted with or at risk for an immunologic disorder."

In applying therapies based on T cell costimulatory molecules, in vitro and even animal model studies have not correlated well with in vivo clinical trial results in patients. Since the efficacy of therapeutic polypeptides can be species- and model-dependent, it is unpredictable whether reliance on the experimental observations in the in vitro experimental results described in the instant specification provide the basis for employing the recited polypeptides to inhibit lymphocyte proliferation in vivo. For example, Blazar et al. (J. Immunol., 1996, 157: 3250 – 3259; see entire document, in particular, e.g. page 3257, column 2 first paragraph) disclose that issues such as tissue distribution, half-life, affinity and avidity obtained with various reagents targeting costimulatory molecules might prove to be highly important in achieving a therapeutic effect. Therefore, any conclusion regarding the efficacy of costimulatory modulation on altering in vivo immune response should be interpreted in light of the specific reagent used (Blazar et al., see page 3257, column 2, paragraph 1). Thus there is no evidence that the experimental model used in the experiments disclosed in the specification would be predictive of the therapeutic methods encompassed by the claims.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Further, the burden of enabling the prevention of a disease (i.e. in a mammal at risk for an immunologic disorder) would be greater than that of enabling a treatment due to the need to screen those subjects susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to immunologic disorders within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently recited compounds in preventing these disease states. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

In view of insufficient guidance by the instant specification and the lack of predictability of the art to which the invention pertains with respect to B7-H3 signaling pathway, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of the clinical protocols, and absent working examples providing evidence that the claimed methods are effective in affecting lymphocyte proliferation in vivo, or in treating any immunological disorders.

11. Claims 1 and 4 – 9 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of the claimed method, because Applicant is not in possession of a "B7-H3 receptor."

Applicant has not disclosed any structural or functional features of a "B7-H3 receptor," therefore, the skilled artisan cannot envision the molecules encompassed by the instant claim language. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

The written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. at 1106.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently,

Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

12. Conclusion: no claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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December 3, 2007